

EFFECT OF DROPERIDOL, FENTANYL, AND THALAMONAL * ON THE THRESHOLD OF MYOCARDIAL ISCHEMIA

M. P. Yakushev, Yu. B. Rozonov,
and T. V. Morozova

UDC 616.127-005.4-092-02:
[615.214.22+615:212.3

KEY WORDS: neuroleptanalgesia, myocardial ischemia threshold, therapy.

Neuroleptanalgesia is widely used for relieving the pain syndrome in acute myocardial infarction [3]. However, the fact that the drugs used have different kinds of action (analgesic, neuroleptic, α -adrenolytic, etc.) leads to diversity of the response both of the hemodynamics as a whole and of the blood supply to the heart in particular. The present investigation was devoted to a study of the action of neuroleptanalgesic agents on the threshold of myocardial ischemia induced by measured coronary occlusion.

EXPERIMENTAL METHOD

Experiments were carried out on 15 waking rabbits of both sexes weighing 2-3 kg. Under pentobarbital anesthesia (40 mg/kg, intravenously) and under artificial respiration, an elastic kapron thread, connected to a device allowing measured constriction of the lumen of the vessel, was passed around the anterior descending branch of the left coronary artery. The degree of occlusion was estimated in degrees on the circular scale of the apparatus. After the immediate after-effects of operative trauma had disappeared, the animals were used in the experiments. At the beginning of the experiment the degree of occlusion of the coronary artery giving stable elevation of the S-T segment on the ECG was determined, i.e., the initial threshold of myocardial ischemia. After normalization of the ECG the drugs were injected and occlusion of the coronary artery was again induced. Altogether 12 series of experiments were undertaken, with seven experiments in each series. The test drugs were injected intravenously: droperidol in doses of 2.5-100 μ g/kg, fentanyl 0.1-2 μ g/kg, and thalamonal (2.5 + 0.1)-(100 + 2) μ g/kg. The ECG was recorded in chest leads III and IV on the Mingograph-82 instrument. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Elevation of the myocardial ischemia threshold ($10.5 \pm 2.7\%$) through the action of droperidol in a dose of 2.5 μ g/kg was recorded in four of seven experiments, and in the rest tolerance of the myocardium to ischemia was unchanged. Injection of the neuroleptic in doses of 5 and 10 μ g/kg caused an increase in resistance of the myocardium to ischemia in all experiments on average by 35.0 ± 8.9 and $51.5 \pm 6.1\%$ respectively. However, with a further increase in the dose of droperidol (to 100 μ g/kg) changes in the threshold of myocardial ischemia differed again: In three experiments it was raised, in two it was unchanged, and in two it was lowered a little.

Injections of fentanyl in a dose of 0.1 μ g/kg caused no increase in the resistance of the myocardium to ischemia. The threshold of ischemia after injection of fentanyl (a narcotic analgesic) in a dose of 0.2 μ g/kg was lower than initially in two cases, unchanged in four, and only in one experiment was it raised by 12.5%. After injection of fentanyl in doses of 1-2 μ g/kg a tendency was observed for the resistance of the myocardium to ischemia to fall on average by 14.9 ± 7.6 and $6.9 \pm 2.9\%$.

After simultaneous injection of droperidol 2.5 μ g/kg and fentanyl 0.1 μ g/kg, the greatest increase in myocardial tolerance to ischemia was observed ($63.8 \pm 15.1\%$). Thalamonal, in constituent doses of droperidol and

*Thalamonal is a combination of droperidol and fentanyl - Translator.

Department of Pharmacology, Kemerovo Medical Institute. Laboratory of Pharmacology of the Cardiovascular System, Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR A. V. Val'dman.) Translated from *Byulleten Éksperimental'noi Biologii i Meditsiny*, Vol. 97, No. 6, pp. 693-694, June, 1984. Original article submitted July 12, 1983.

fentanyl of 5 ± 0.2 and 10 ± 1 $\mu\text{g/kg}$, raised the threshold of ischemia by 51.6 ± 6.2 and $56.7 \pm 15.0\%$. Changes in the ischemia threshold after injection of droperidol and fentanyl in high doses (100 ± 2 $\mu\text{g/kg}$) were varied in direction: In two experiments the threshold of myocardial ischemia rose, in three it was unchanged, and in two it fell to 12 and 50%.

The writers showed previously that droperidol increases the coronary blood flow in acute coronary occlusion, lowers the central venous pressure and peripheral vascular resistance, and also causes redistribution of the myocardial flow for the benefit of the endocardium [4, 5]. Elevation of the ischemia threshold by droperidol in waking animals can thus be regarded as the result of improvement of the blood supply to the diseased heart. This effect of the drug is probably associated not only with its central and peripheral α -adrenolytic action [1], but also with a direct lytic effect on the coronary arteries. The possibility cannot be ruled out that a definite role in the increase of myocardial tolerance to ischemia is played by a reduction in the pre-load and after-load on the affected heart. With an increase in the dose of droperidol its hypotensive effect is potentiated, and this impairs the blood supply to the ischemic heart. The smaller rise in the threshold of myocardial ischemia under the influence of droperidol 100 $\mu\text{g/kg}$ compared with the action of small doses of the drug is evidently connected with this.

Fentanyl also increased the volume velocity of the coronary blood flow, but it increased by an even greater degree the oxygen consumption of the affected myocardium. It can be tentatively suggested that lowering of the threshold of myocardial ischemia by fentanyl is connected with aggravation of the oxygen deficiency in the heart. The depressant effect of the analgesic on the animals' respiratory center may also play a definite role [2].

Elevation of the threshold of myocardial ischemia by thalamonal in small doses of its constituent preparations probably develops on account of realization of the cardiovascular effect of droperidol with their potentiation by fentanyl, the mechanism of which calls for special investigation. The relatively smaller increase in myocardial tolerance to ischemia following combined injection of droperidol and fentanyl in high doses (100 and 2 $\mu\text{g/kg}$) is evidently due to the ability of droperidol to induce marked hypotension, which cancels out its lytic action on the coronary arteries, and the unfavorable effect of large doses of fentanyl on the oxygen balance of the infarcted heart.

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